

CORRECTED VERSION

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
27 January 2005 (27.01.2005)

PCT

(10) International Publication Number  
**WO 2005/007635 A2**

(51) International Patent Classification<sup>7</sup>: **C07D 261/00**

(21) International Application Number:  
PCT/IT2004/000373

(22) International Filing Date: 6 July 2004 (06.07.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
RM 2003 A 000355 18 July 2003 (18.07.2003) IT

(71) Applicant (for all designated States except US):  
**SIGMA-TAU INDUSTRIE FARMACEUTICHE RIUNITE S.p.A.** [IT/IT]; Viale Shakespeare, 47, I-00144 Roma (IT).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **SIMONI, Daniele**

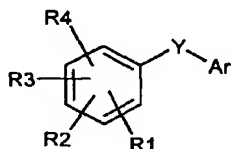
[IT/IT]; c/o Simgma-Tau Industrie Farmaceutiche Riunite S.p. .A., Via Pontina, Km. 30,400, I-00040 Pomezia (IT). **ROMAGNOLI, Romeo** [IT/IT]; c/o Simgma-Tau Industrie Farmaceutiche Riunite S.p. .A., Via Pontina, Km. 30,400, I-00040 Pomezia (IT). **GIANNINI, Giuseppe** [IT/IT]; c/o Simgma-Tau Industrie Farmaceutiche Riunite S.p. .A., Via Pontina, Km. 30,400, I-00040 Pomezia RM (IT). **ALLOATTI, Domenico** [IT/IT]; c/o Simgma-Tau Industrie Farmaceutiche Riunite S.p. .A., Via Pontina, Km. 30,400, I-00040 Pomezia RM (IT). **PISANO, Claudio** [IT/IT]; c/o Sigma-Tau Industrie Farmaceutiche Riunite S.p. .A., Via Pontina, Km. 30,400, I-00040 Pomezia RM (IT).

(74) Agent: **SPADARO, Marco**; Cavattoni - Raimondi, Viale dei Parioli, 160, I-00197 Roma (IT).

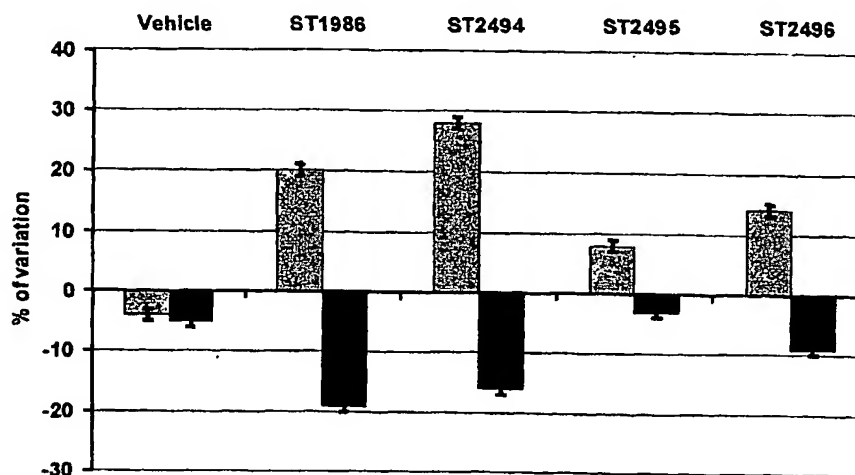
(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,

[Continued on next page]

(54) Title: **COMBRETASTATIN DERIVATIVES WITH CYTOTOXIC ACTION**



(I)



(57) Abstract: The invention described herein relates to new combretastatin derivatives obtained by total synthesis and having the following general formula (I) in which the groups are as defined in the description here below. Said compounds, though chemically related to the structure of cis/trans-combretastatin, do not always bind tubulin, but nevertheless exhibit cytotoxic activity of interest in the oncological field as anticancer and/or antiangiogenic agents.



GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

- (84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— *without international search report and to be republished upon receipt of that report*

- (48) **Date of publication of this corrected version:**

12 May 2005

- (15) **Information about Correction:**

see PCT Gazette No. 19/2005 of 12 May 2005, Section II

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*